**NON-TECHNICAL ABSTRACT**

This is a first-time use of a method of gene therapy designed to transfer anti-HIV genes into the blood stems cells of AIDS patients who have a poor prognosis lymphoma for which they have chosen to undergo a type of bone marrow transplantation called autologous (from oneself) hematopoietic cell transplantation (HCT). The aim is to introduce anti-HIV genes into the blood stem cells at the time of the HCT and to see if these cells can safely grow in the patient and express the anti-HIV genes. The gene transfer to the stem cells will be done using a "vector" that was made from HIV by removing most of the viral genes and substituting the antiviral genes. This vector, called rHIV7-shI-TAR-CCR5RZ, encodes three genes that, when processed in the cell, will make a chemical called RNA of three types known to inhibit HIV: 1) an interfering RNA (RNAi) that blocks two essential HIV genes called tat and rev (shI), 2) an RNA that mimics and competes with the an HIV protein necessary to make new copies of HIV (TAR), and 3) an RNA called "ribozyme" that decreases a normal cell protein important for infection with HIV (CCR5RZ). The genetically modified stem cells used for the HCT are the research agent for this study. This is primarily a safety study, and subjects will be followed for side effects of the procedure. But subjects will also be followed for evidence that the gene-modified cells have engrafted and have made new blood cells that circulate and express the transferred genes as RNA molecules, suggesting the potential for these new blood cells to have become resistant to HIV infection. In addition, the study will seek to determine whether the transferred genes have become part of the research participants' own genome by integrating into DNA and whether the participants' own HIV-1 isolates might have mixed with the rHIV7-shI-TAR-CCR5RZ vector to form a new HIV virus, an event that could alter the nature of the virus in potentially good or bad ways.

Patients with AIDS lymphoma, who agree to participate, will have of their blood stem cells collected and frozen prior during the course of standard lymphoma chemotherapy. A portion of these cells will be genetically modified using the rHIV7-shI-TAR-CCR5RZ vector, and an equal portion of cells will remain otherwise unmanipulated to provide the cells needed for the standard-of-care HCT. Then, at the time of HCT, the genetically modified stem cells will be infused first, and the next day, the unmanipulated cells will be given. The subjects will be followed for side effects of this procedure and, after the cells engraft, blood specimens will be analyzed for evidence that the transferred genes are expressed as RNA in circulating blood cells or in bone marrow cells. Also, the site of transgene integration into normal DNA will be determined, and the patient's own HIV will be tested to see if it as been changed by the treatment. The results of this study will answer the question of whether this new strategy of gene therapy deserves further evaluation as an eventual method for control of HIV.